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NOTICE OF ALLOWANCE AND FEE(S) DUE

22852 7590 02/19/2004

FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER
LLP
1300 I STREET, NW
WASHINGTON, DC 20005

EXAMINER	
SPEAR, JAMES M	
ART UNIT	**PAPER NUMBER**
1615	

DATE MAILED: 02/19/2004

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/642,160	08/21/2000	Bent Hojgaard	06063.0019	7752

TITLE OF INVENTION: PHARMACEUTICAL DELIVERY SYSTEM FOR VITAMIN C AND VITAMIN E AND USE OF A COMBINATION OF VITAMIN C AND E FOR PREVENTING OR TREATING CONDITIONS INVOLVING OXIDATIVE STRESS

APPLN. TYPE	SMALL ENTITY	ISSUE FEE	PUBLICATION FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	NO	$1330	$0	$1330	05/19/2004

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE REFLECTS A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE APPLIED IN THIS APPLICATION. THE PTOL-85B (OR AN EQUIVALENT) MUST BE RETURNED WITHIN THIS PERIOD EVEN IF NO FEE IS DUE OR THE APPLICATION WILL BE REGARDED AS ABANDONED.

HOW TO REPLY TO THIS NOTICE:

I. Review the SMALL ENTITY status shown above.

If the SMALL ENTITY is shown as YES, verify your current SMALL ENTITY status:
A. If the status is the same, pay the TOTAL FEE(S) DUE shown above.

B. If the status is changed, pay the PUBLICATION FEE (if required) and twice the amount of the ISSUE FEE shown above and notify the United States Patent and Trademark Office of the change in status, or

If the SMALL ENTITY is shown as NO:

A. Pay TOTAL FEE(S) DUE shown above, or

B. If applicant claimed SMALL ENTITY status before, or is now claiming SMALL ENTITY status, check the box below and enclose the PUBLICATION FEE and 1/2 the ISSUE FEE shown above.

☐ Applicant claims SMALL ENTITY status. See 37 CFR 1.27.

II. PART B - FEE(S) TRANSMITTAL should be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). Even if the fee(s) have already been paid, Part B - Fee(s) Transmittal should be completed and returned. If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed and an extra copy of the form should be submitted.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.

PTOL-85 (Rev. 11/03) Approved for use through 04/30/2004.

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), to: Mail **Mail Stop ISSUE FEE**
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INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 4 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

CURRENT CORRESPONDENCE ADDRESS (Note: Legibly mark-up with any corrections or use Block 1)

22852 7590 02/19/2004

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Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

Certificate of Mailing or Transmission

I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being facsimile transmitted to the USPTO, on the date indicated below.

(Depositor's name)

(Signature)

(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/642,160	08/21/2000	Bent Hojgaard	06063.0019	7752

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nonprovisional	NO	$1330	$0	$1330	05/19/2004

EXAMINER	ART UNIT	CLASS-SUBCLASS
SPEAR, JAMES M	1615	424-458000

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).

❑ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.

❑ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list (1) the names of up to 3 registered patent attorneys or agents OR, alternatively, (2) the name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.

1 _____

2 _____

3 _____

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. Inclusion of assignee data is only appropriate when an assignment has been previously submitted to the USPTO or is being submitted under separate cover. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE (B) RESIDENCE: (CITY and STATE OR COUNTRY)

Please check the appropriate assignee category or categories (will not be printed on the patent); ❑ individual ❑ corporation or other private group entity ❑ government

4a. The following fee(s) are enclosed:

❑ Issue Fee

❑ Publication Fee

❑ Advance Order - # of Copies _____

4b. Payment of Fee(s):

❑ A check in the amount of the fee(s) is enclosed.

❑ Payment by credit card. Form PTO-2038 is attached.

❑ The Director is hereby authorized by charge the required fee(s), or credit any overpayment, to Deposit Account Number _____ (enclose an extra copy of this form).

Director for Patents is requested to apply the Issue Fee and Publication Fee (if any) or to re-apply any previously paid issue fee to the application identified above.

(Authorized Signature) (Date)

NOTE; The Issue Fee and Publication Fee (if required) will not be accepted from anyone other than the applicant; a registered attorney or agent; or the assignee or other party in interest as shown by the records of the United States Patent and Trademark Office.

This collection of information is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, Alexandria, Virginia 22313-1450.

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TRANSMIT THIS FORM WITH FEE(S)

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22852 7590 02/19/2004

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EXAMINER	
SPEAR, JAMES M	

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 02/19/2004

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)
(application filed on or after May 29, 2000)

The Patent Term Adjustment to date is 0 day(s). If the issue fee is paid on the date that is three months after the mailing date of this notice and the patent issues on the Tuesday before the date that is 28 weeks (six and a half months) after the mailing date of this notice, the Patent Term Adjustment will be 0 day(s).

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) system (http://pair.uspto.gov).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (703) 305-1383. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at (703) 305-8283.

PTOL-85 (Rev. 11/03) Approved for use through 04/30/2004.

Notice of Allowability	Application No.	Applicant(s)	
	09/642,160	HOJGAARD ET AL.	
	Examiner	Art Unit	
	James M Spear	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *THE AMENDMENT FILED December 23, 2003*.

2. ☒ The allowed claim(s) is/are *38,39,46-50,57,58,60,67,69-71 and 74*.

3. ☒ The drawings filed on *28 August 2000* are accepted by the Examiner.

4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

6. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

7. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO-1449 or PTO/SB/08), Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application (PTO-152)
6. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____ .
7. ☐ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

James M. Spear

James M Spear
Primary Examiner
Art Unit: 1615

1. The following is an examiner's statement of reasons for allowance:

a. Applicants show a delivery system comprised of slow release vitamin C and plain release vitamin E and a method of treating oxidative stress disorders with said delivery system. The prior art shows modified release compositions comprised of vitamin C and vitamin E. Valducci EP 0 820 703 A1, considered the closest prior art of record, shows prolonged release formulations comprised of these vitamins. The prior art does not show nor fairly suggest applicants' particular combination of slow release vitamin C and plain release vitamin E, wherein vitamin C is present in an amount to deliver a daily dose of 60 mg to 2 gm vitamin C and vitamin E is present in an amount to deliver 50 mg to 500 mg alpha tocopherol. The vitamins are present in amounts so as to obtain vitamin C and vitamin E in a ratio in the blood plasma of 1:1 to 3:1 such that the delivery system provides a concentration of vitamin E in the blood plasma of at least 20 micro moles per liter and a concentration of vitamin C in the blood plasma of at least 40 micro moles per liter.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Claims 38, 39, 46-50, 57, 58, 60, 67, 69-71 and 74 are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James M Spear whose telephone number is 571

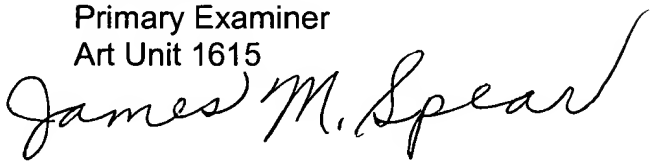
272 0605. The examiner can normally be reached on Monday thru Friday from 6:30 AM to 3 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page, can be reached on 571 272 0602. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

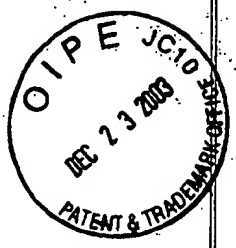
Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

James M Spear
Primary Examiner
Art Unit 1615

February 12, 2004



61



AF/1615

BOX AF
RESPONSE UNDER 37 C.F.R. 1.116
EXPEDITED PROCEDURE
EXAMINING GROUP 1610

PATENT
Customer No. 22,852
Attorney Docket No. 06063.0019

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	)	
	)	
Bent HØJGAARD et al.	)	
	)	
Application No.: 09/642,160	)	Group Art Unit: 1615
	)	
Filed: August 21, 2000	)	Examiner: J. SPEAR

For: A PHARMACEUTICAL DELIVERY SYSTEM FOR VITAMIN C AND VITAMIN E AND USE OF A COMBINATION OF VITAMIN C AND E FOR PREVENTING OR TREATING CONDITIONS INVOLVING OXIDATIVE STRESS

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

AMENDMENT AFTER FINAL REJECTION UNDER 37 C.F.R. § 1.116

Sir:

In response to the Final Office Action mailed September 23, 2003, Applicants request that this application be amended as follows.

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IN THE CLAIMS:

Please amend claim 46 as indicated in the following claim listing:

~~38.~~ (Previously Presented) A delivery system for oral delivery of the antioxidants vitamin C and vitamin E to obtain high concentrations thereof and a controlled ratio between vitamin C and vitamin E in blood plasma in humans or animals, characterized in that it has a slow release of vitamin C and a plain release of vitamin E;

wherein vitamin C is present in an amount in the delivery system so as to deliver a daily dose corresponding to 60 mg - 2 g of vitamin C, and vitamin E is present in an amount in the delivery system so as to deliver a daily dose corresponding to 50 mg - 500 mg of α-tocopherol, and the antioxidants are present in amounts so as to obtain vitamin C and vitamin E in a ratio in the blood plasma of 1:1 to 3:1;

wherein the solubility of vitamin E is such that at least 90% of vitamin E is dissolved in less than 30 minutes under the conditions of Test B; and

wherein the solubility of vitamin C is such that less than 40% of vitamin C is dissolved after 1 hour under the conditions of Test A; and

wherein said delivery system achieves a concentration of vitamin E in the blood plasma of at least 20 μmol/liter and a concentration of vitamin C in the blood plasma of at least 40 μmol/liter.

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2 ~~39.~~ (Previously Presented) A delivery system according to claim 1 ~~38~~, characterized in that it is a system comprising a tablet comprising at least two non-identical delivery principles, wherein

a) one delivery principle comprises

i) vitamin C;

ii) a pharmaceutically acceptable excipient for controlling the slow release of vitamin C; and

iii) other pharmaceutically acceptable excipients; and

b) another delivery principle comprises

i) vitamin E; and

ii) pharmaceutically acceptable excipients.

3 ~~46.~~ (Currently Amended) A delivery system according to claim 1 ~~38~~, characterized in that vitamin C is ascorbic acid and vitamin E is selected from ~~the group comprising~~ d-α-tocopheryl acetate, d-α-tocopheryl acid succinate, d-α-tocopherol, d-β-tocopherol, d-γ-tocopherol, d-δ-tocopherol, d-α-tocotrienol, d-β-tocotrienol, d-γ-tocotrienol, d-δ-tocotrienol, dl-α-tocopherol, dl-α-tocopheryl acetate, dl-α-tocopheryl calcium succinate, dl-α-tocopheryl nicotinate, dl-α-tocopheryl linoleate/oleate, and ~~all other possible~~ derivatives or stereo isomeric forms of the above compounds.

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4 ~~47~~. (Previously Presented) A delivery system according to claim ~~38~~ 1, wherein the daily dose of vitamin C corresponds to 100 mg - 1.5 g of ascorbic acid.

5 ~~48~~. (Previously Presented) A delivery system according to claim ~~38~~ 1, wherein the daily dose of vitamin E corresponds to 100 mg - 250 mg of α-tocopherol.

6 ~~49~~. (Previously Presented) A delivery system according to claim ~~38~~ 1, wherein the daily dose of vitamin C and E is delivered by 1 to 8 dosage units.

7 ~~50~~. (Previously Presented) A delivery system according to claim ~~38~~ 1, wherein the daily dose of vitamin C and E is delivered by 1 or 2 dosage units.

8 ~~51~~. (Previously Presented) A method of treating oxidative stress disorders, said method comprising administering to an individual a combination of vitamin C and vitamin E in sufficient amounts to raise the concentration of said vitamins in blood plasma to a ratio of approximately 1:1 to 3:1, in not more than 8 weeks from the first administration,

wherein vitamin C is released by a slow release formulation and vitamin E is released by a plain release formulation; and

wherein the concentration of vitamin E in the blood plasma is at least 20 μmol/liter and the concentration of vitamin C in the blood plasma is at least 40 μmol/liter; and

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wherein the administering is in amounts corresponding to a daily dose of 60 mg - 2 g of vitamin C and corresponding to a daily dose of 50 mg - 500 mg of α-tocopherol.

9 ~~58.~~ (Previously Presented) A method according to claim 8 ~~57~~, wherein the raising is within 4 weeks.

10 ~~60.~~ (Previously Presented) A method according to claim 8 ~~57~~, wherein the method achieves, in blood plasma, a concentration of vitamin C of from about 102 to 142 μmol/liter, and a concentration of vitamin E of from about 46 to 65 μmol/liter.

11 ~~61.~~ (Previously Presented) A method of treating oxidative stress disorders, said method comprising daily administering to an individual at least one dosage unit comprising a combination of vitamin C and vitamin E in sufficient amounts to raise the concentration of said vitamins in blood plasma to a controlled ratio;

wherein said vitamin C is formulated in a slow-release preparation and vitamin E is formulated only in plain-release formulation;

wherein the concentration of vitamin E in the blood plasma is at least 20 μmol/liter, and the concentration of vitamin C in the blood plasma is at least 40 μmol/liter;

wherein the antioxidants are present in amounts so as to obtain vitamin C and vitamin E in a ratio in the blood plasma of 1:1 to 3:1;

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wherein the at least one dosage units delivers a daily dose corresponding to 60 mg - 2 g of vitamin C and a daily dose corresponding to 50 mg - 500 mg of α-tocopherol; and

wherein the formulation of vitamin E is such that at least 90% of vitamin E is dissolved in less than 30 minutes under the conditions of Test B, and the formulation of vitamin C is such that less than 40% of vitamin C is dissolved after 1 hour under the conditions of Test A.

12 ~~69~~. (Previously Presented) A method according to claim ~~67~~ 11, wherein the method achieves, in blood plasma, a concentration of vitamins C of from about 102 to 142 μmol/liter, and a concentration of vitamin E of from about 46 to 65 μmol/liter.

13 ~~70~~. (Previously Presented) A method according to claim ~~67~~ 11, wherein the at least one dosage unit is at most 8 dosage units.

14 ~~71~~. (Previously Presented) A method according to claim ~~70~~ 13, wherein the at least one dosage unit is 1 or 2 dosage units.

15 ~~74~~. (Previously Presented) A delivery system according to claim ~~38~~ 1, substantially free of histidine.

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